

Fig. 1

(prior art)

Cell

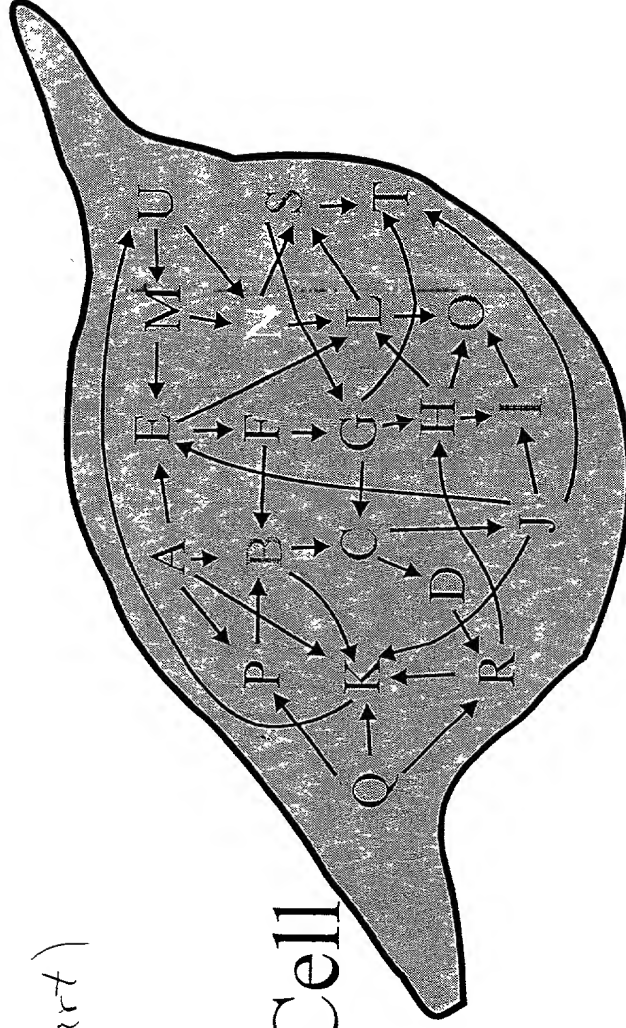


Fig. 2

(prior art)

MAP Kinase/Phosphoinositide/ PI3 Kinase Pathways in the Network

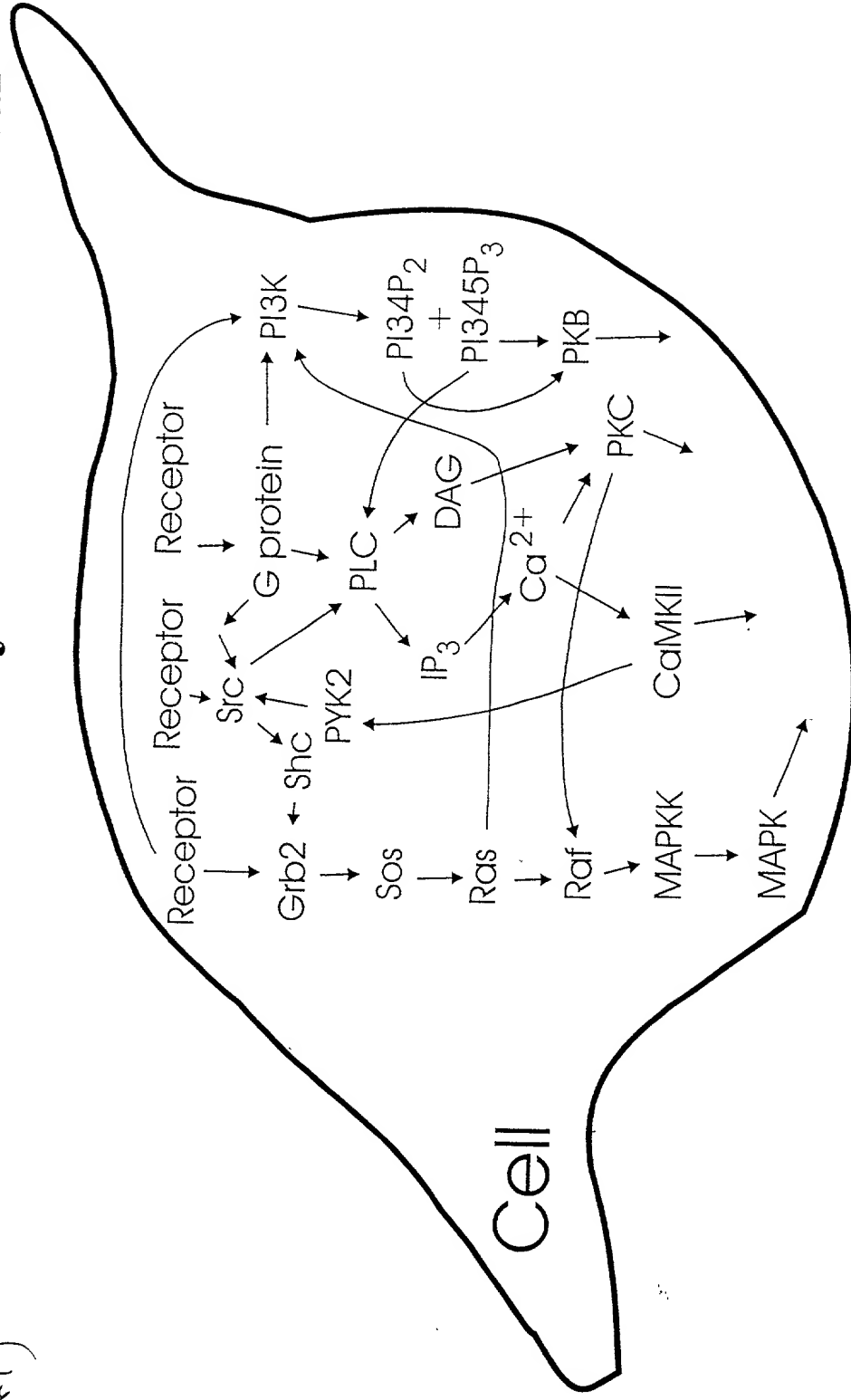


Fig. 3

(prior art)

Measurement of Kinase Activation (Current Technology)

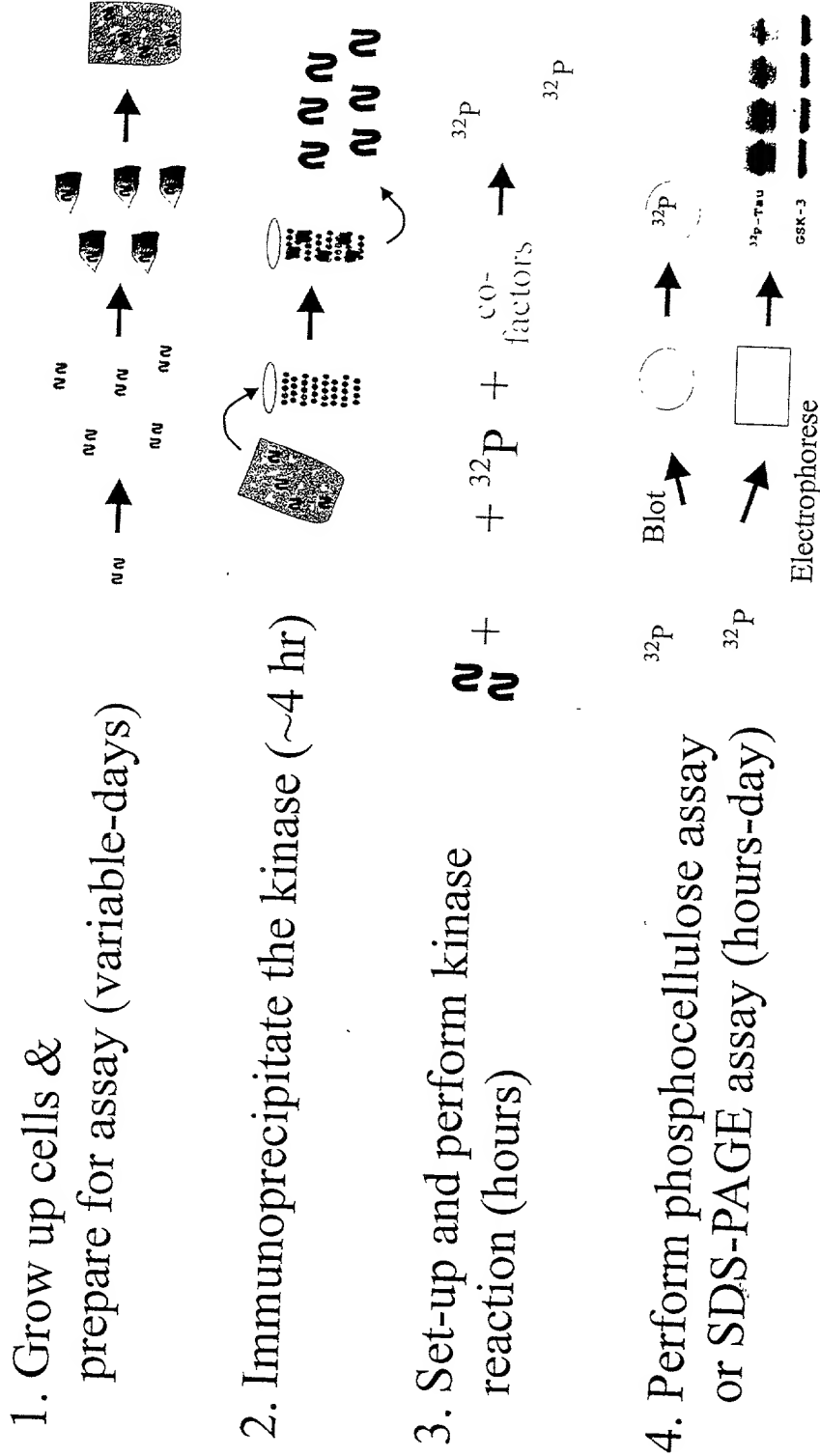
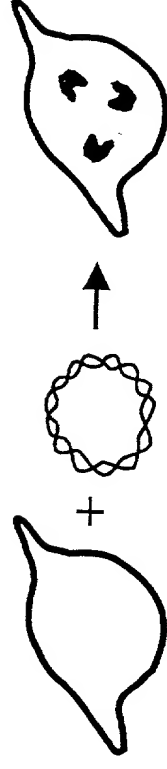


Fig. 4

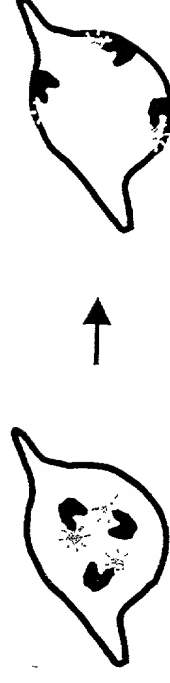
(prior art)

Measurement of Protein Location (via GFP Tag)

1. Develop stably transfected cell lines carrying the overexpressed GFP-tagged protein



2. Fluorescent imaging and pattern recognition

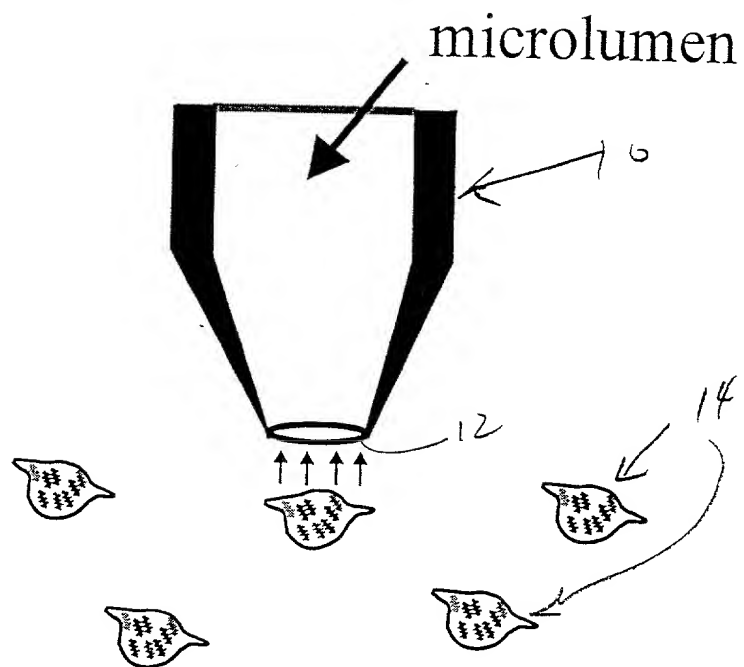


3. Infer protein activity from location

Assay Time ~Minutes

Fig. 5A

Single



Multiple

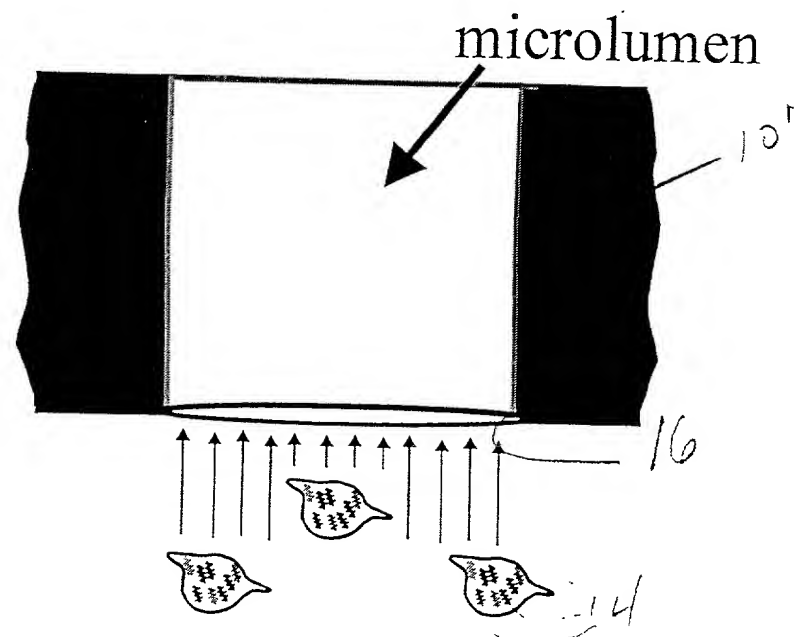
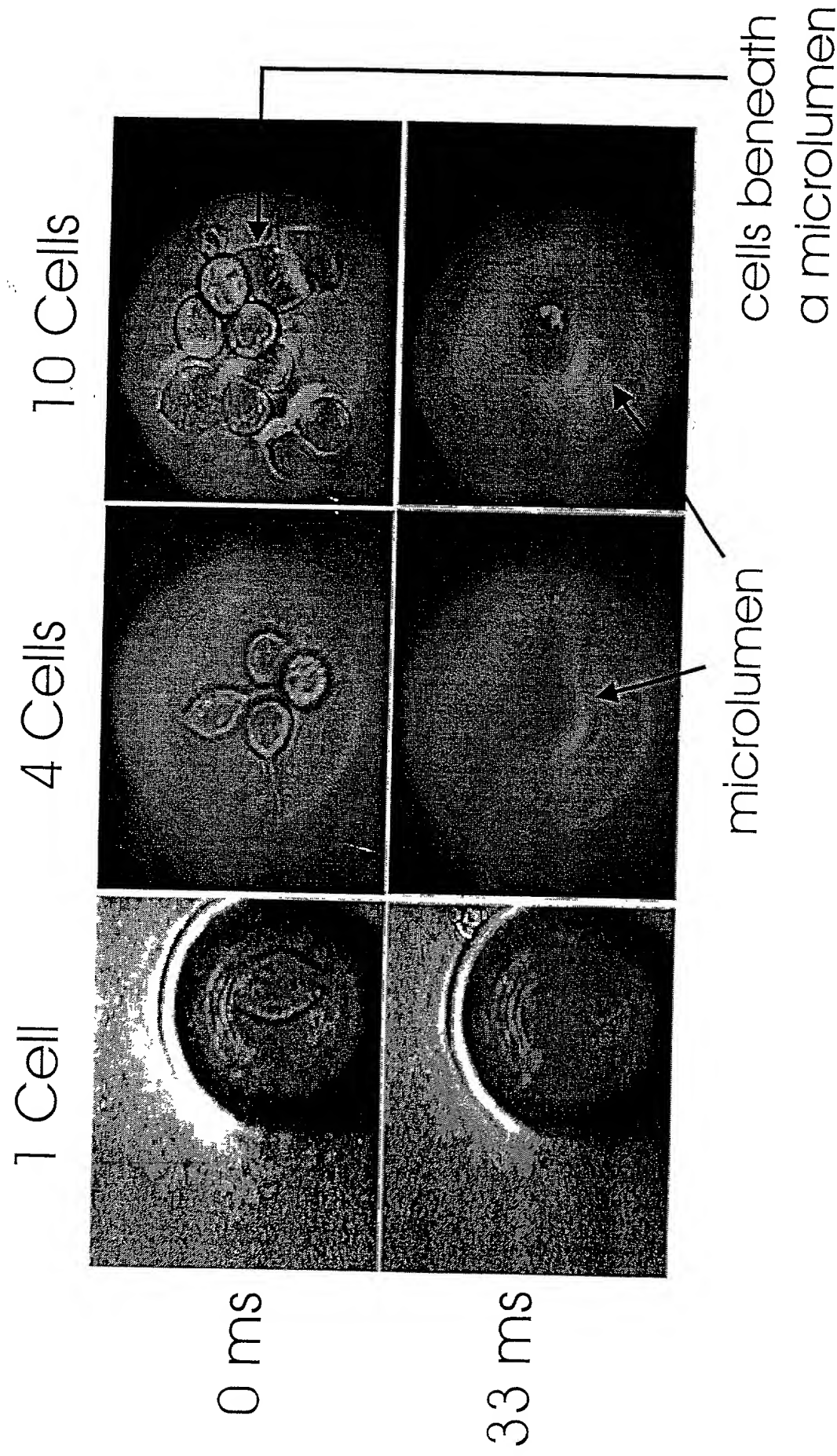


Fig. 5B

Performing "Population Average" Measurements



Single Cells or Population Averages

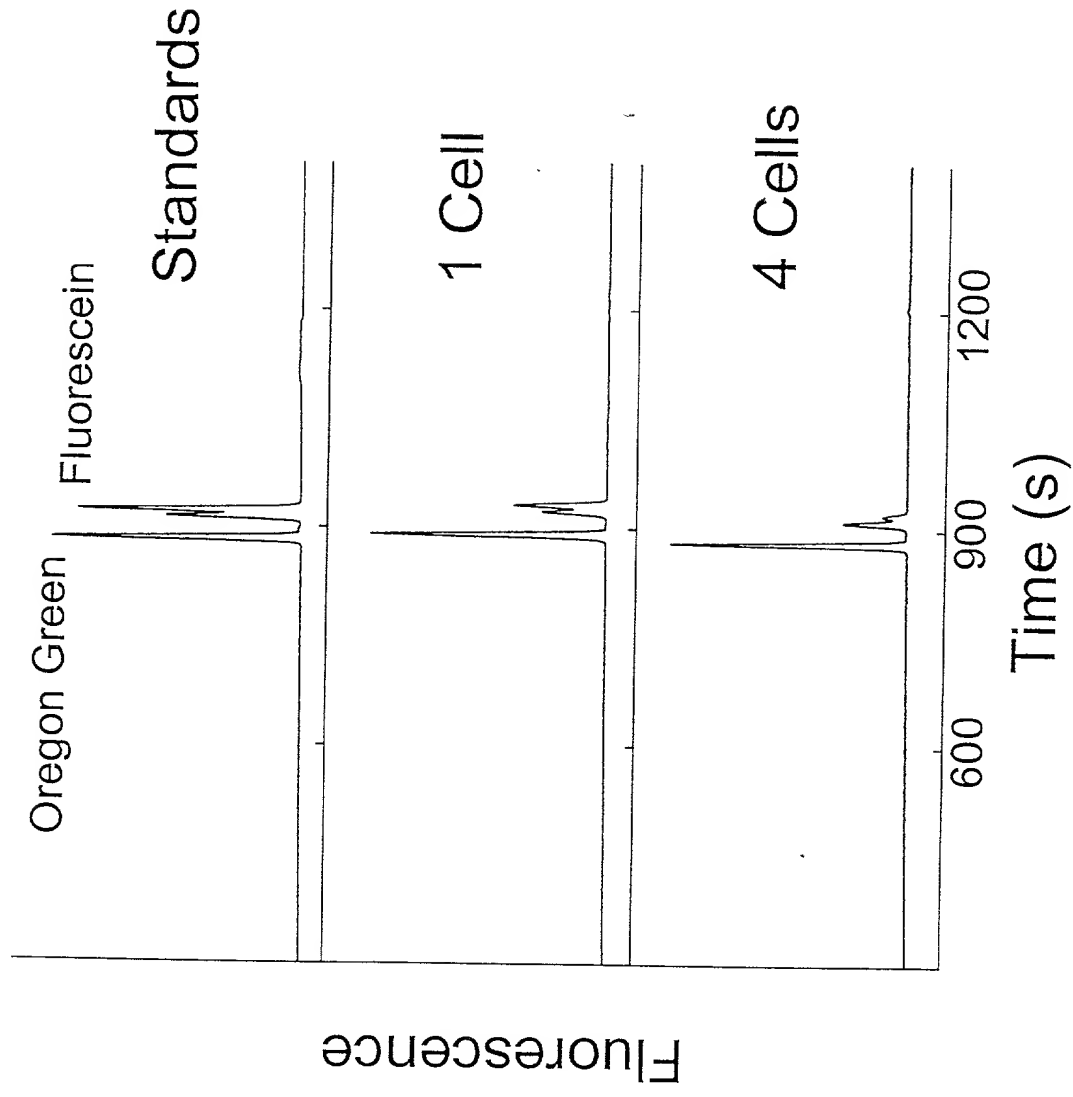


Fig. 5C

Fig. 6A Sampling a Portion of a Cell

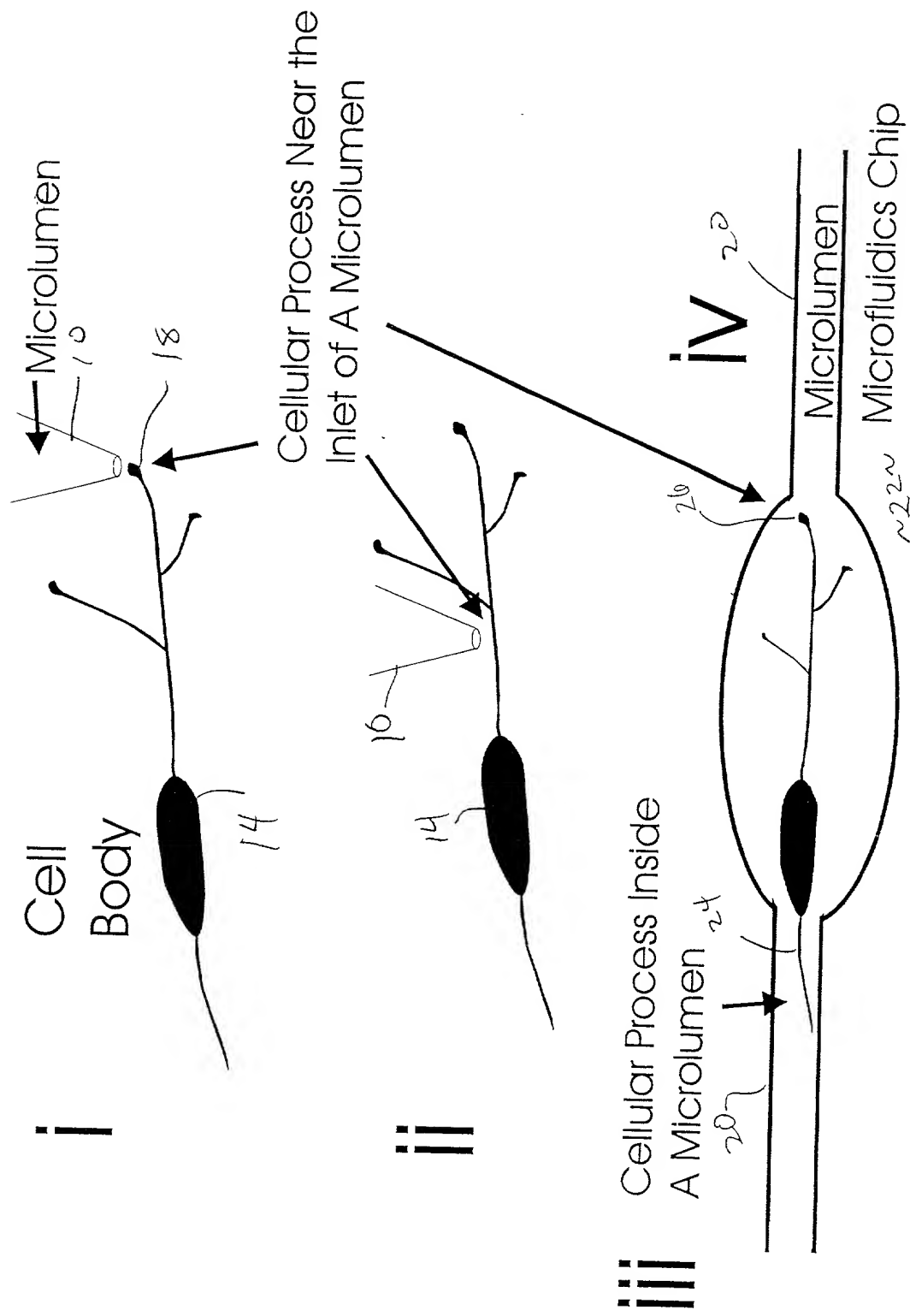


Fig. 6B

Sampling the Contents of a Neuronal Process

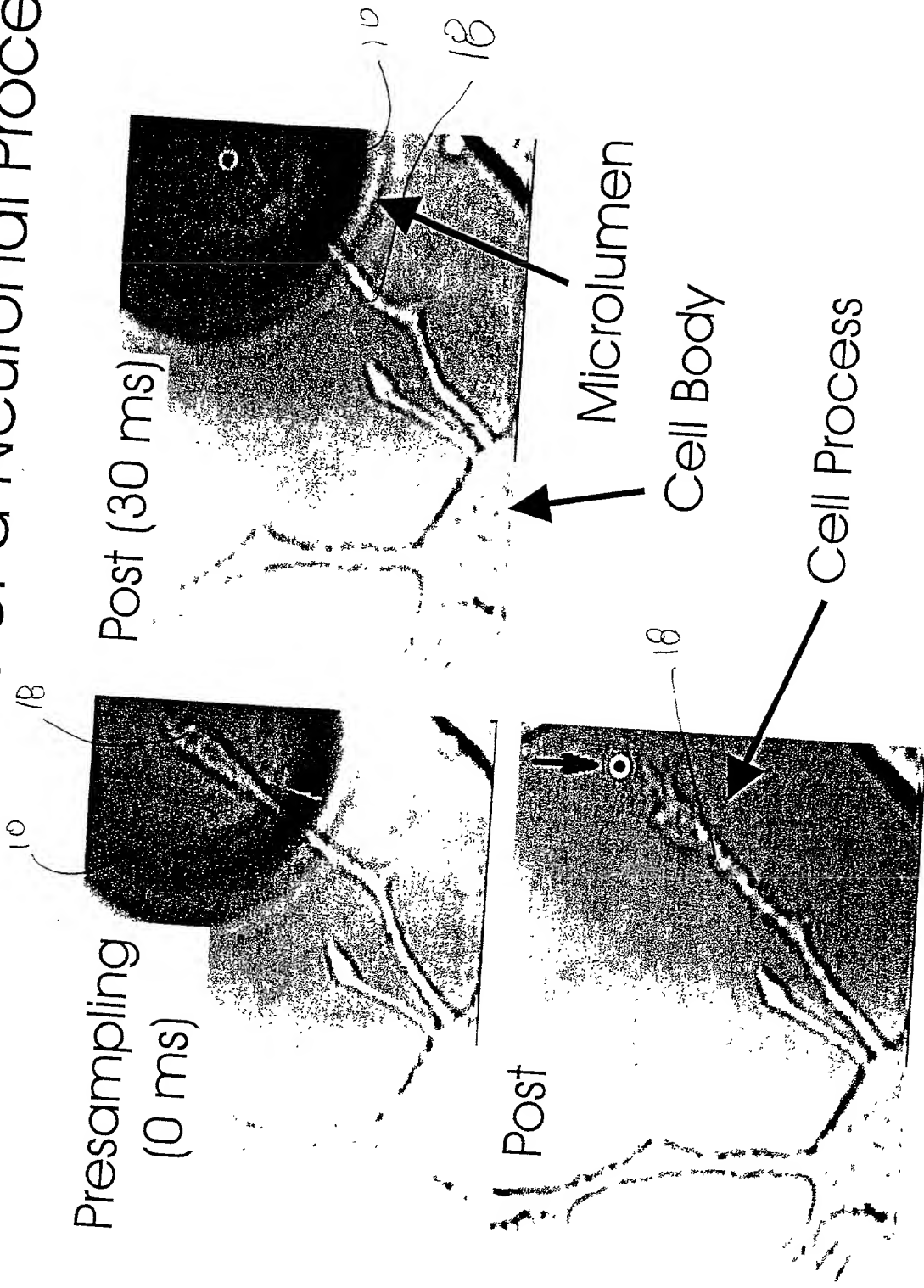


Fig. 6C

Analyzing A Neuronal Process

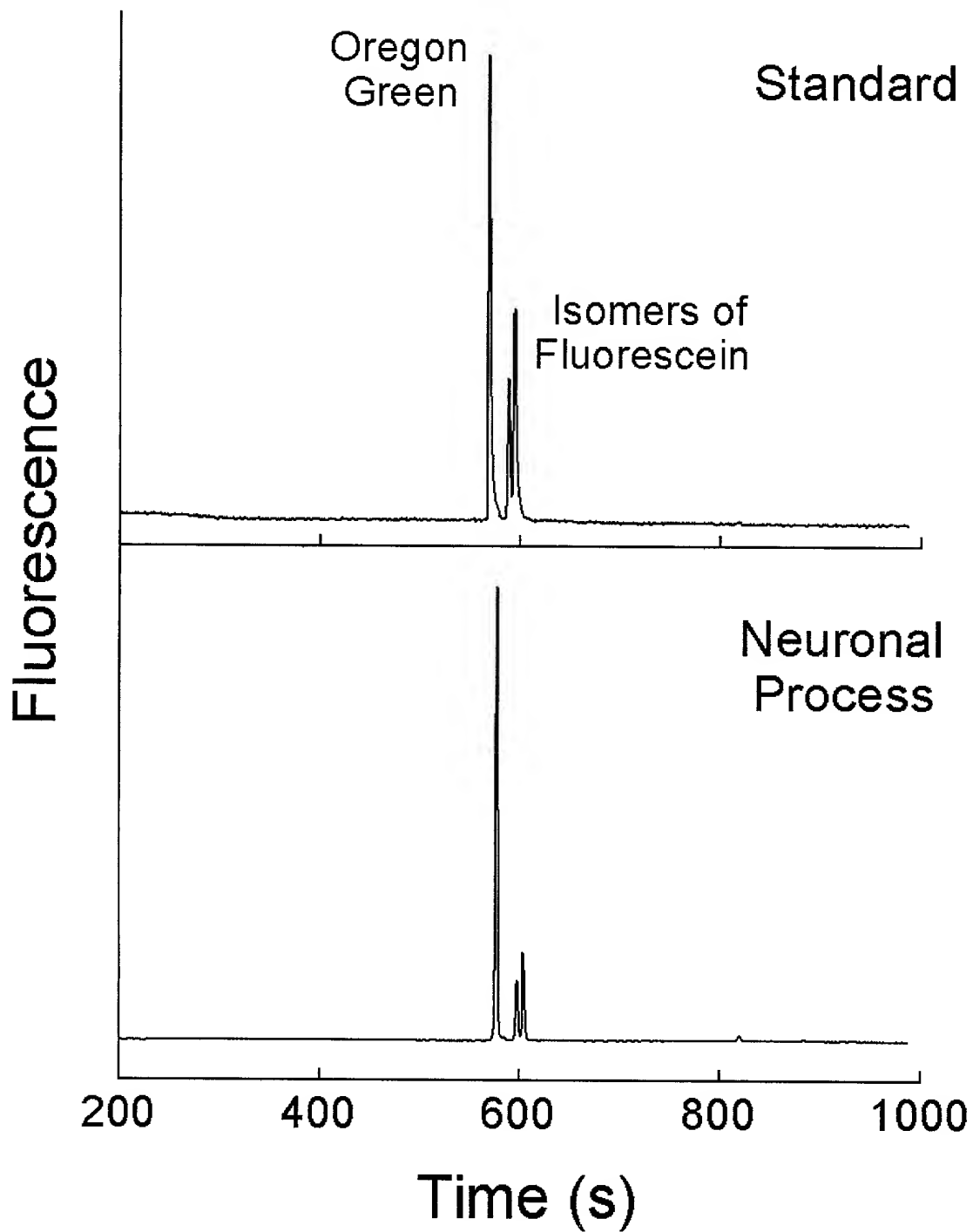


Fig. 7a

Cell Assay

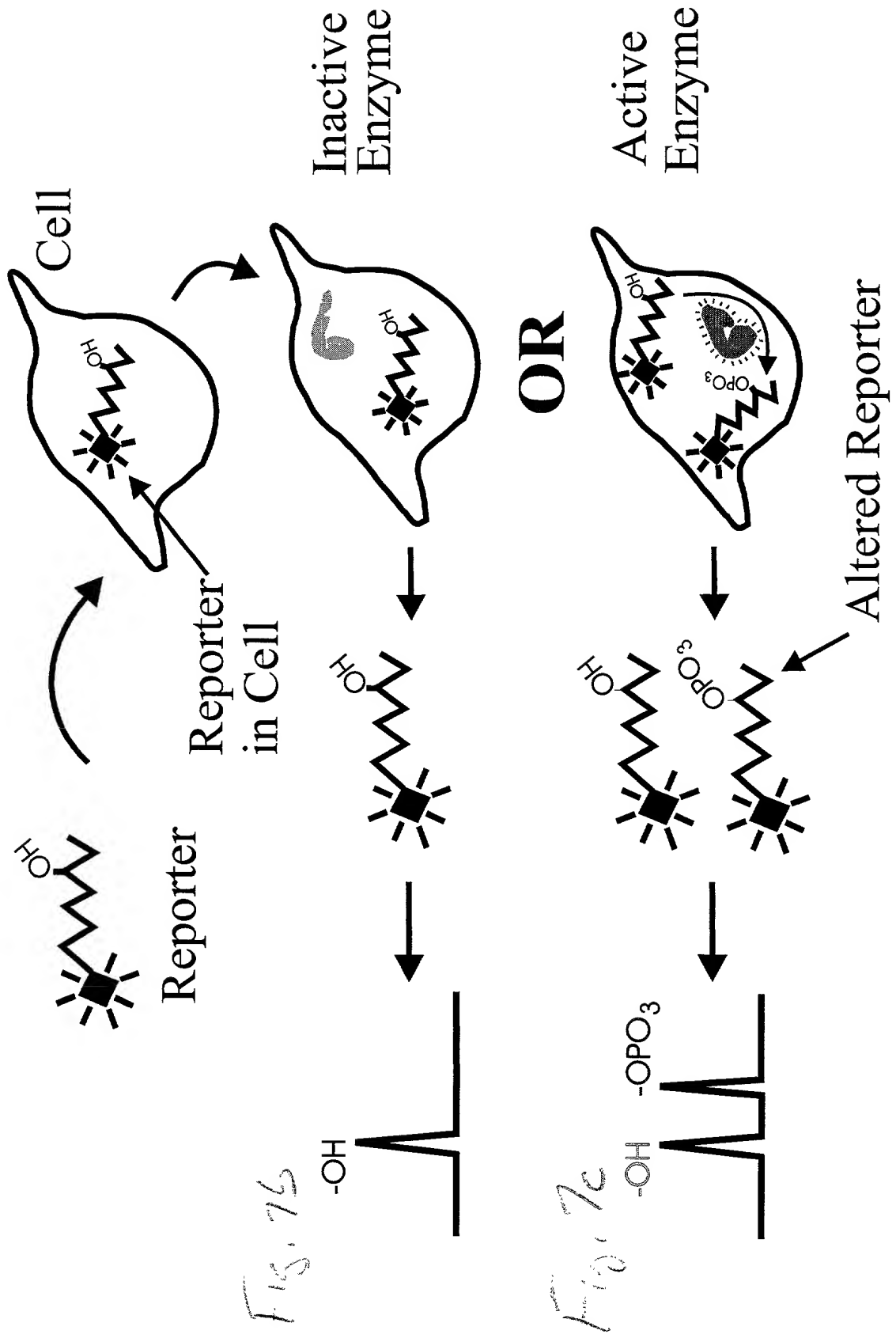
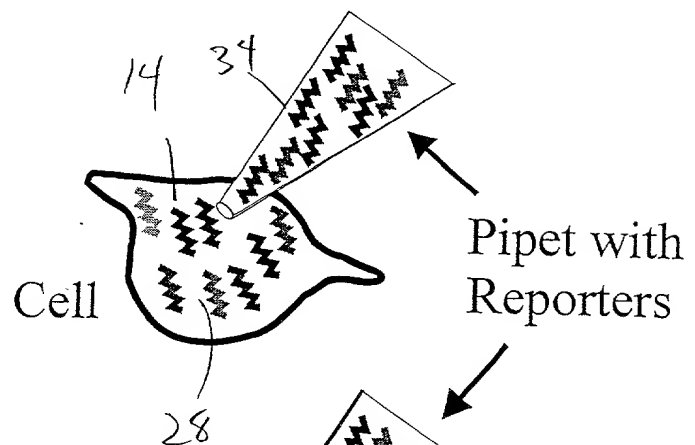


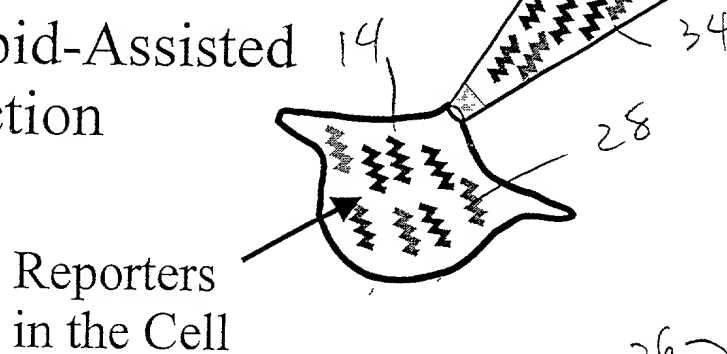
Fig. 8

Loading Single Cells With Enzyme Substrates

Microinjection



Simple Lipid-Assisted
Microinjection



Optoinjection

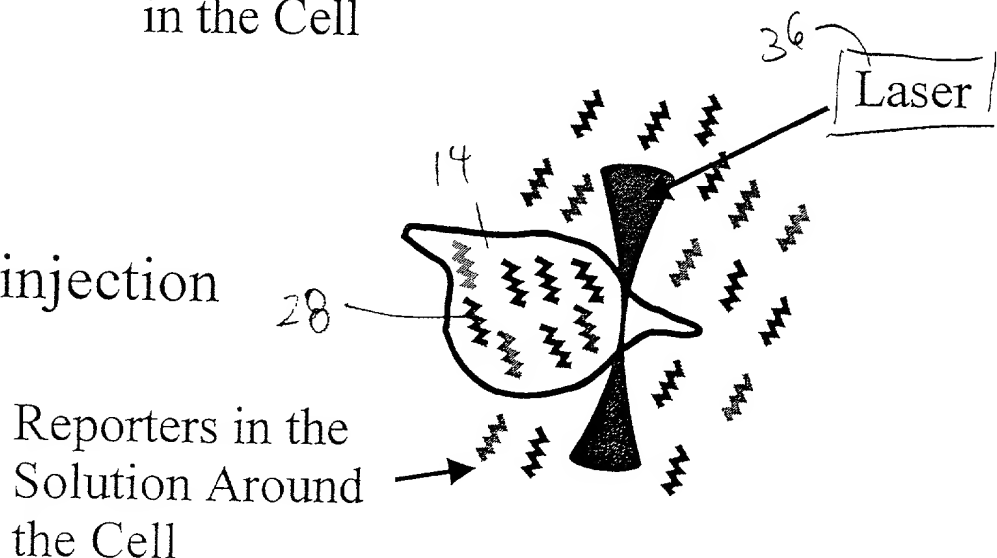
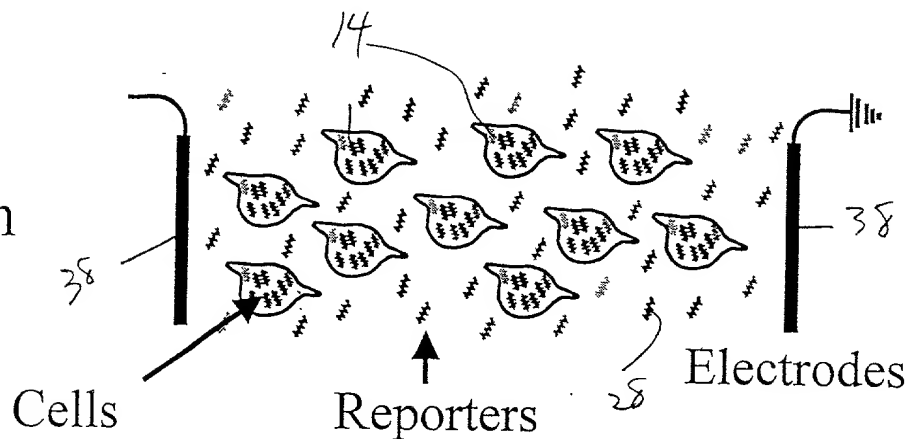
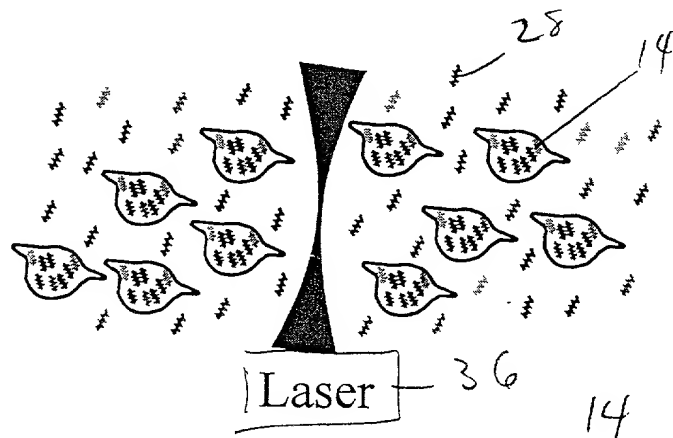


Fig. 9 Loading Multiple Cells With Enzyme Substrates

Electroporation



Optoporation



Passive Techniques

Pinocytosis

Vesicle Fusion

Membrane-Permeant
Substrates

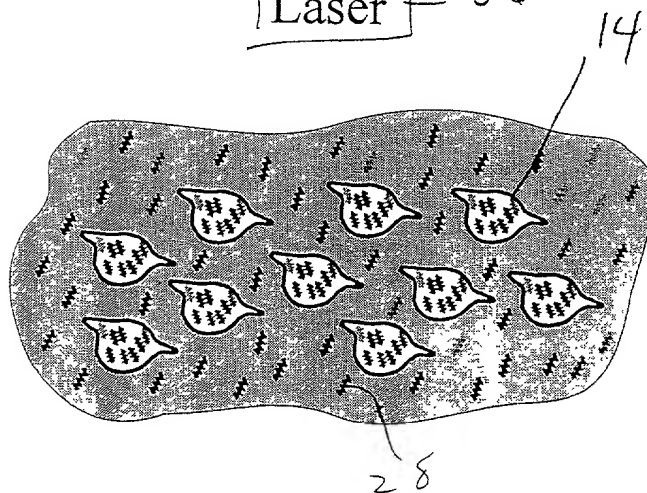
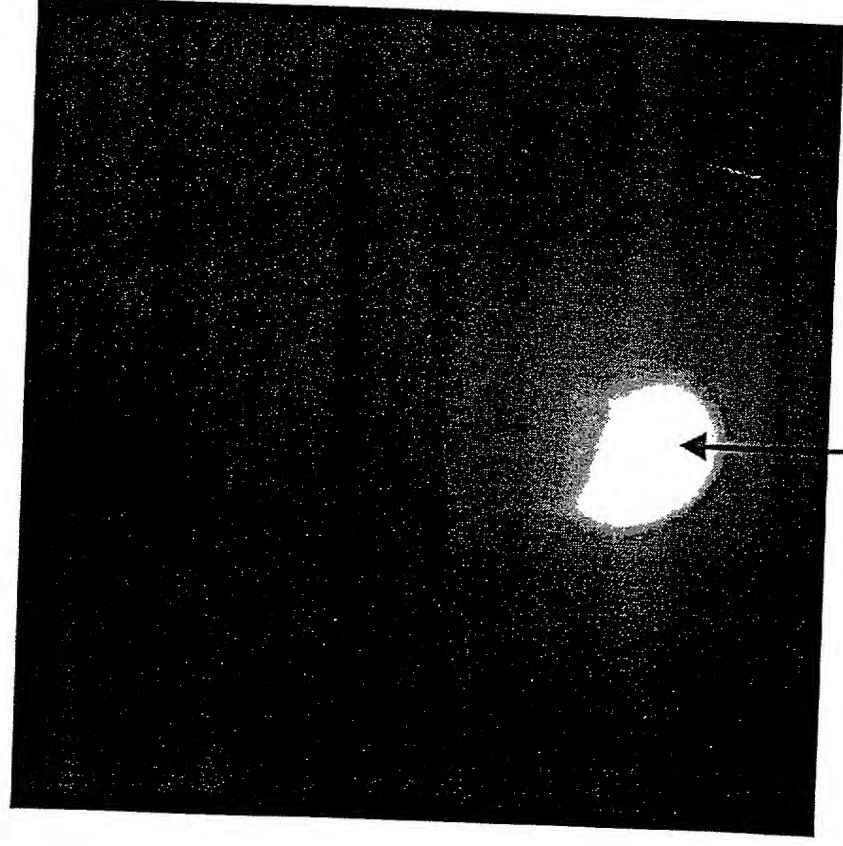


Fig. 10

Nuclear-Localized Substrate for PKC
Fluorescence Image Transmitted Light Image



Nucleus of Cell



Cytoplasm of Cell

Fig. 11

Coupling to Other Technologies

Proteomics

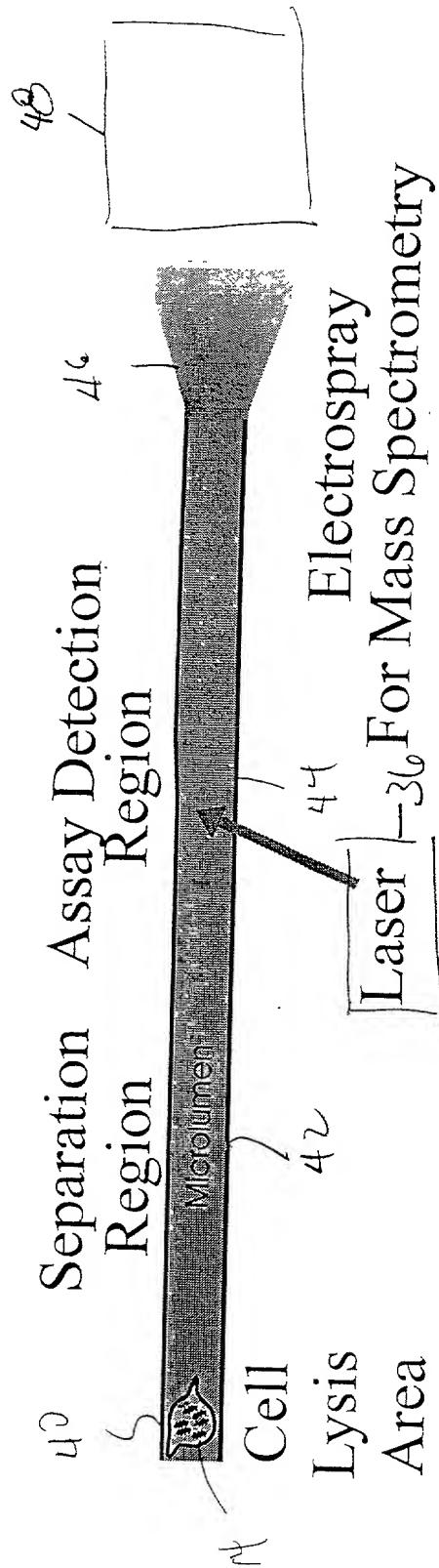


Fig. 12A

Coupling to Other Technologies

Genomics

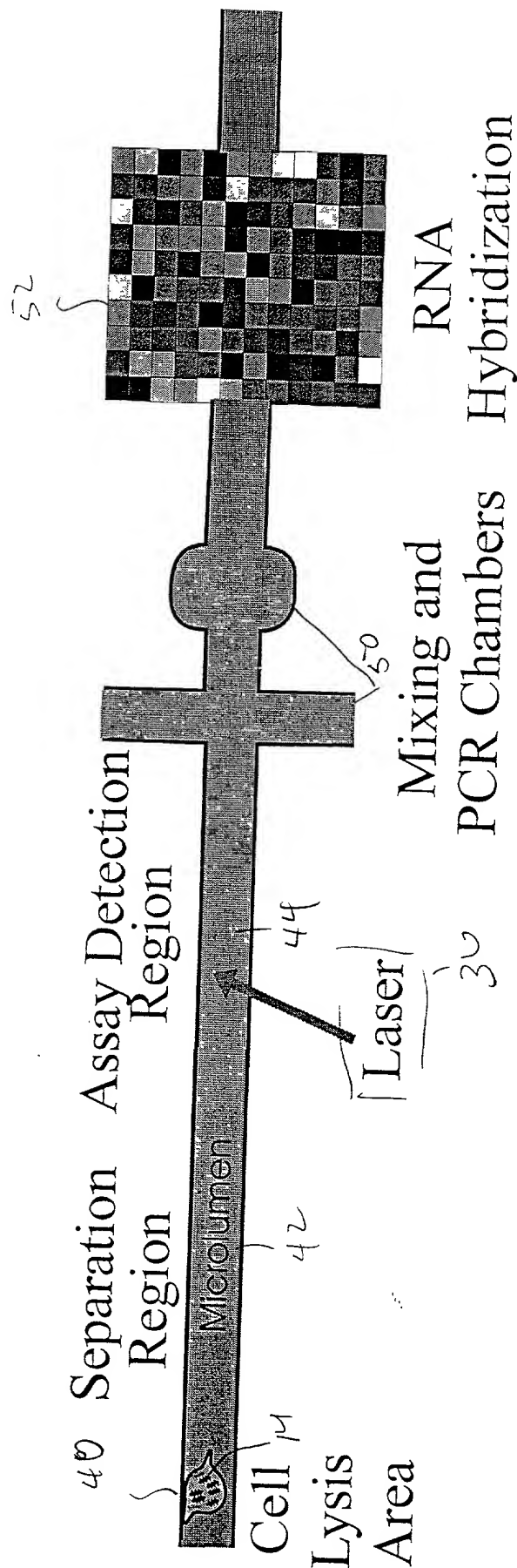


Fig. 12B

SIGNAL TRANSDUCTION MICROCHIP

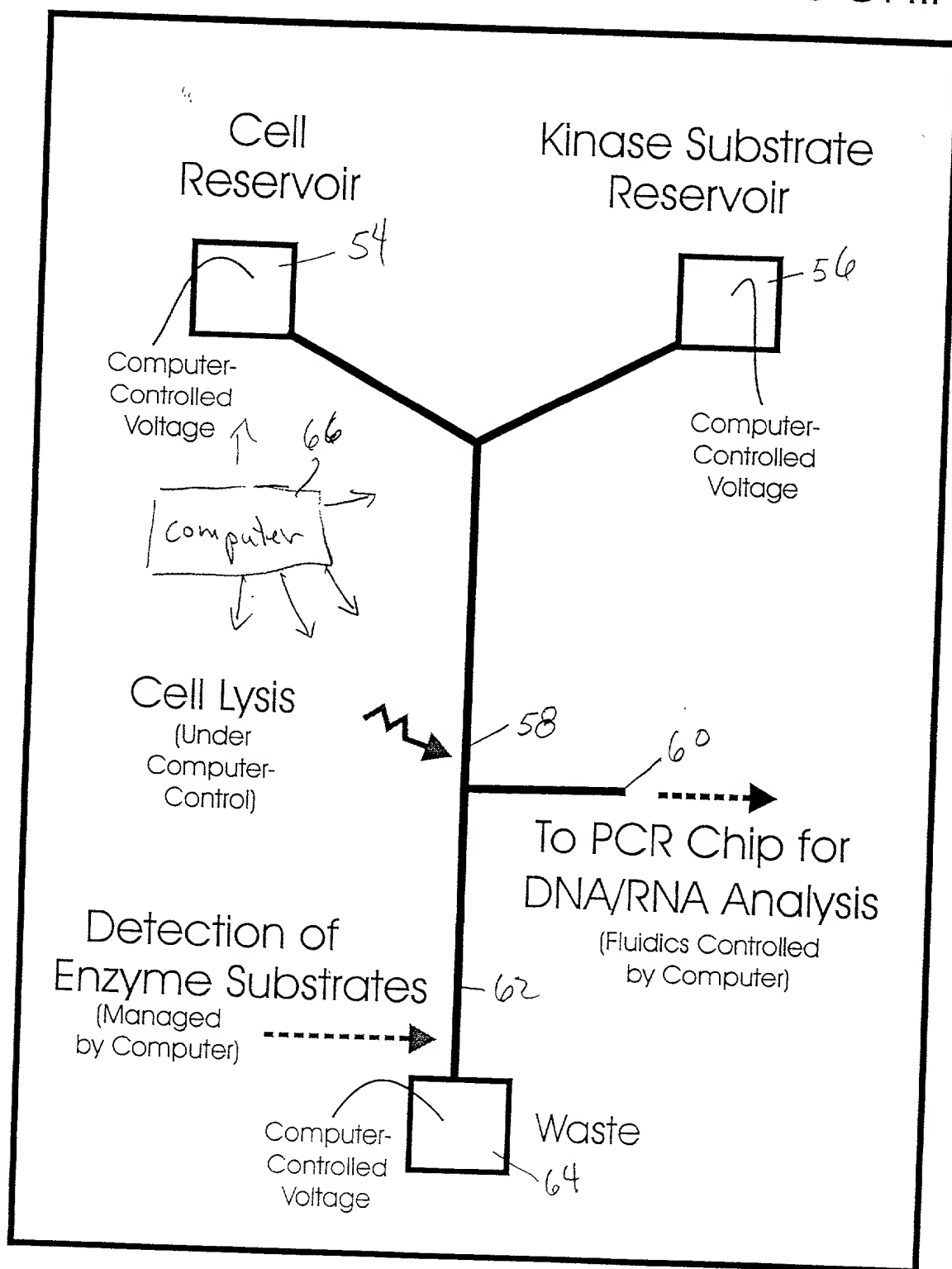


Fig. 13

Coupling to Other Technologies

Flow Cytometry

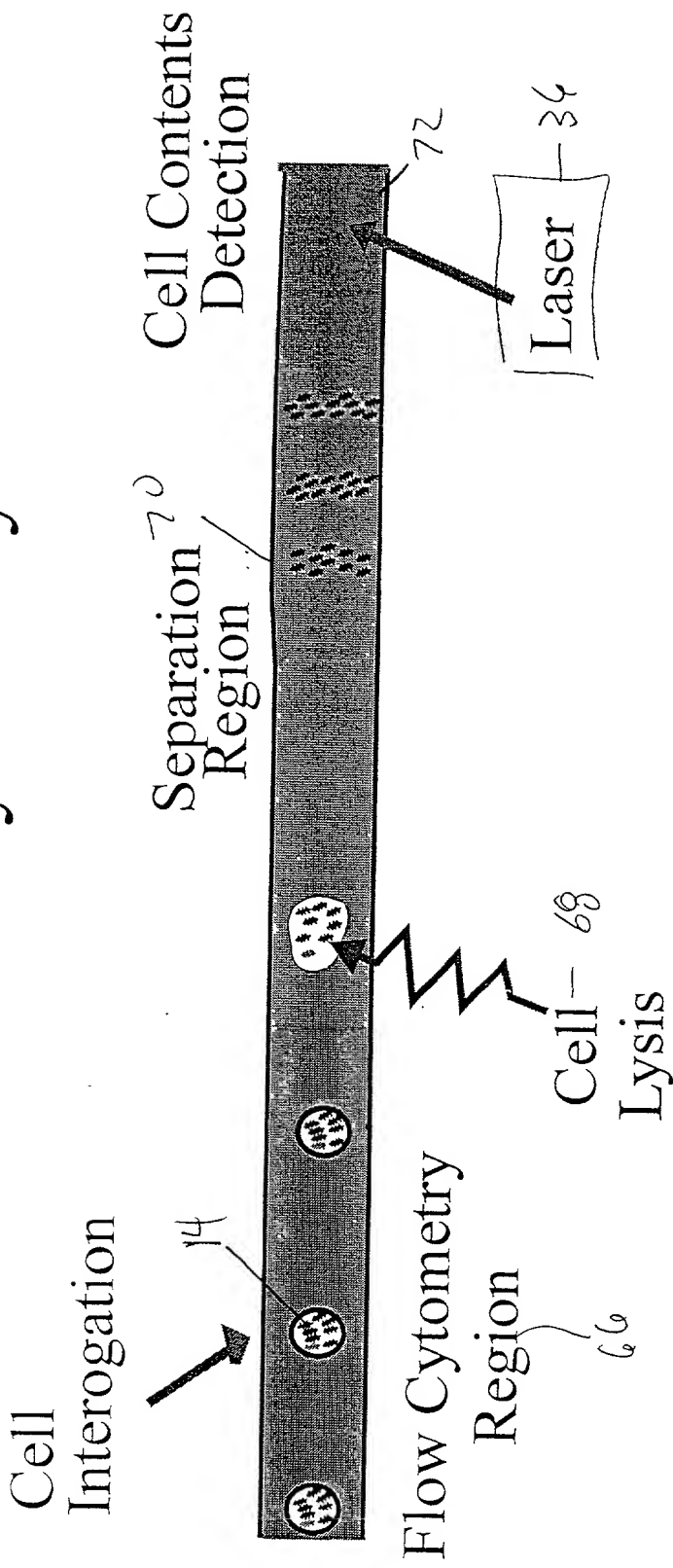
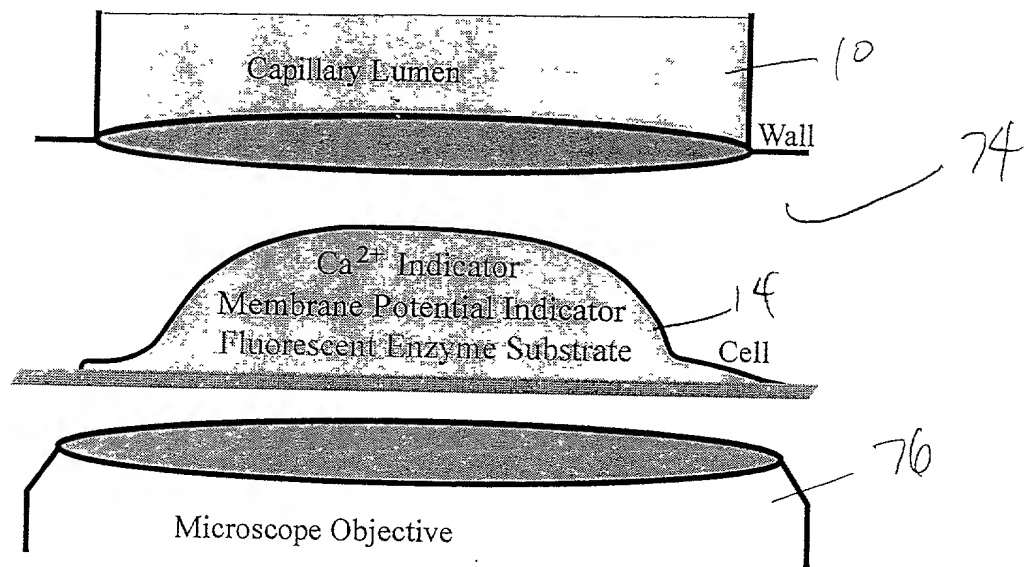


Fig. 14

Integration With Other Cellular Analysis Methods

Fluorescence Imaging



Patch Clamp

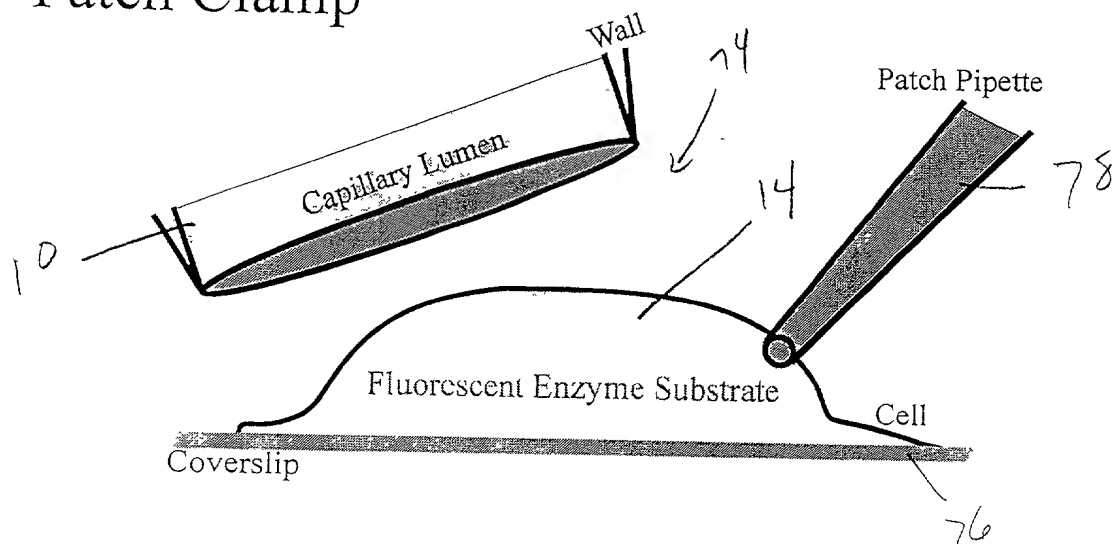
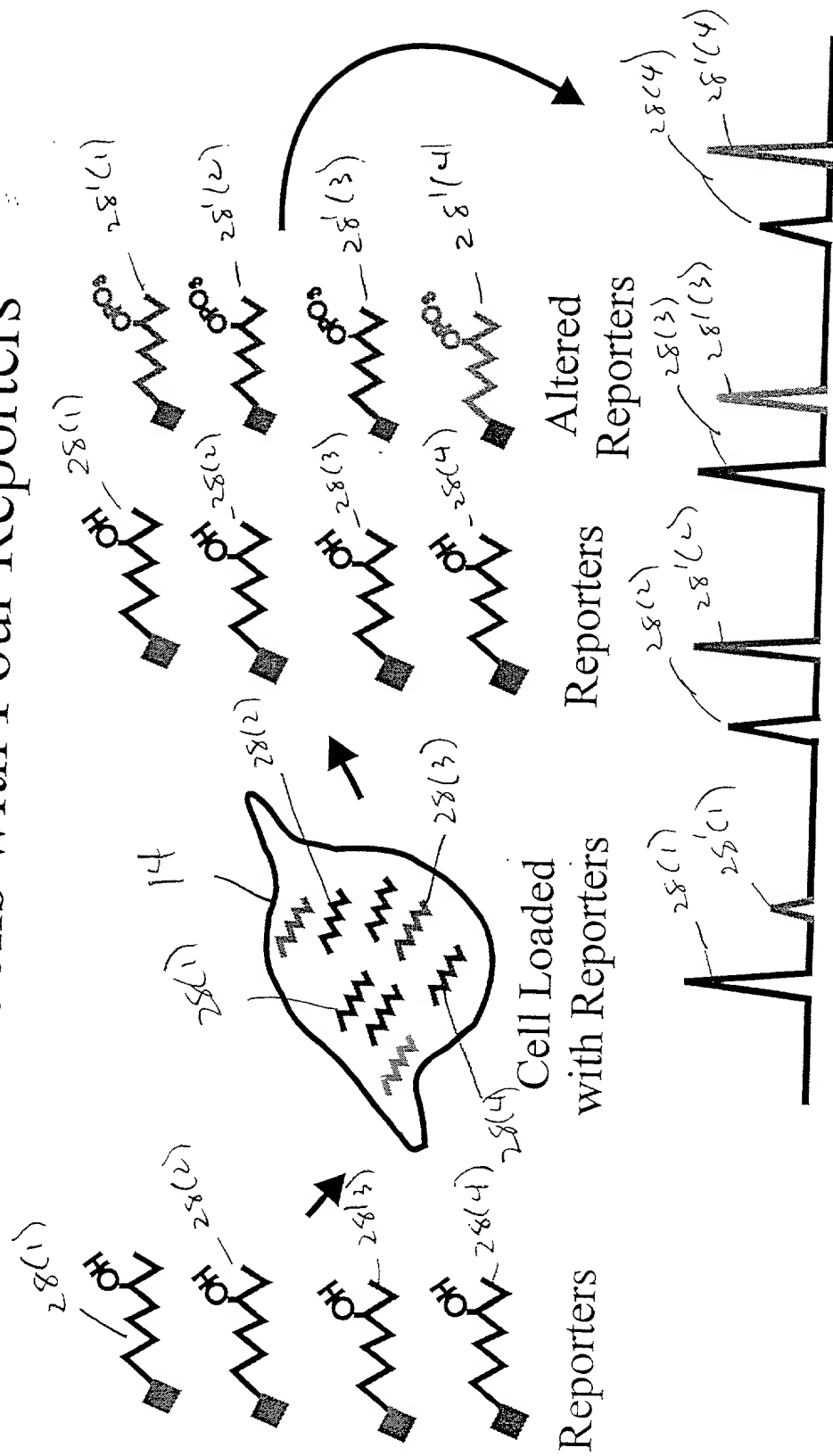


Fig. 15A

Profiling Signal Transduction Pathways in Cells with Four Reporters



Separation of Reporters and Altered Reporters

Fig. 15B

Profiling Signal Transduction Pathways in Cells with Three Reporters

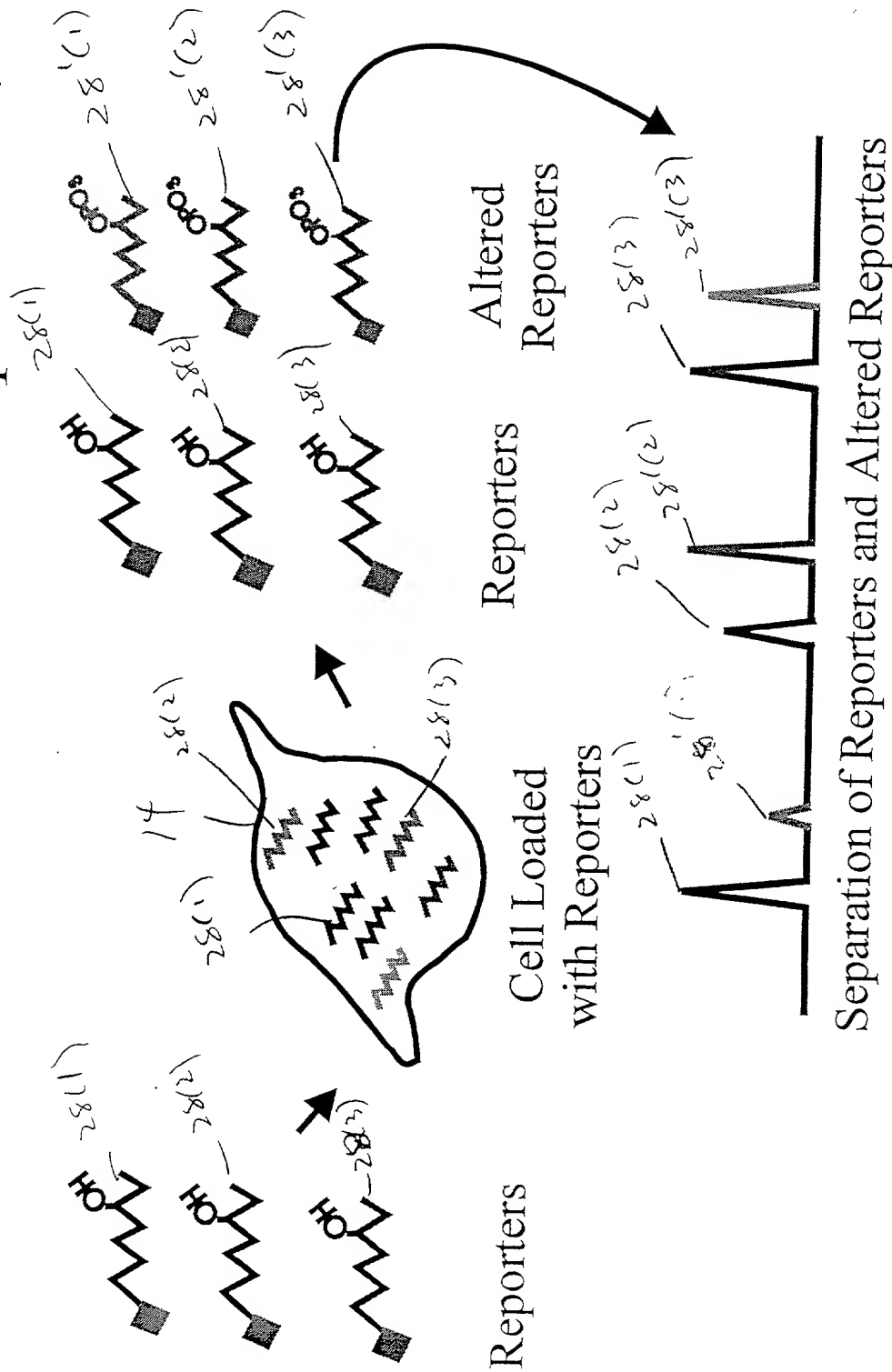


Fig. 16

Profiling Signal Transduction Pathways in Cells with Five Reporters

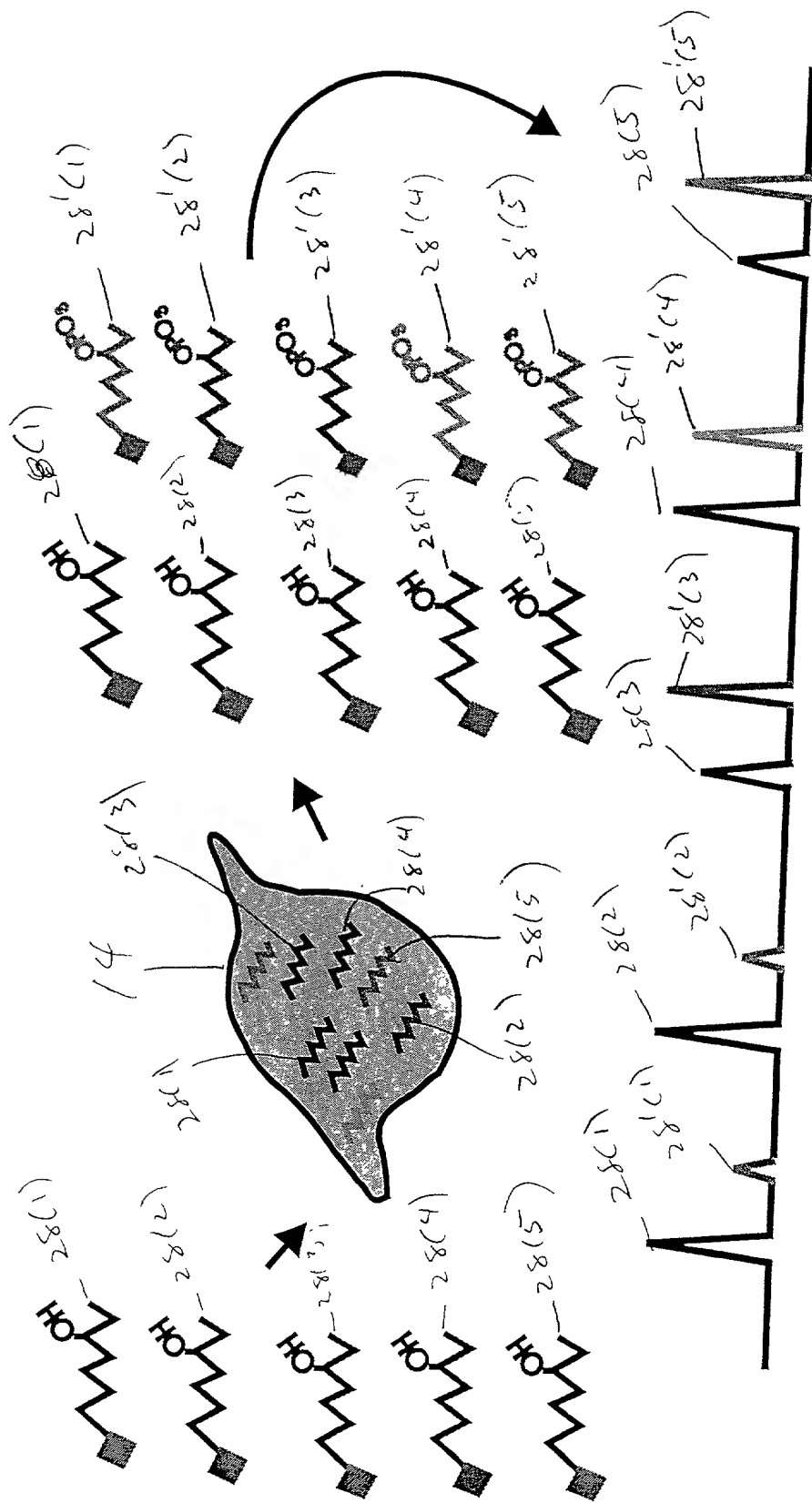


Fig. 17

Profiling Signal Transduction Pathways in Cells with Ten Reporters

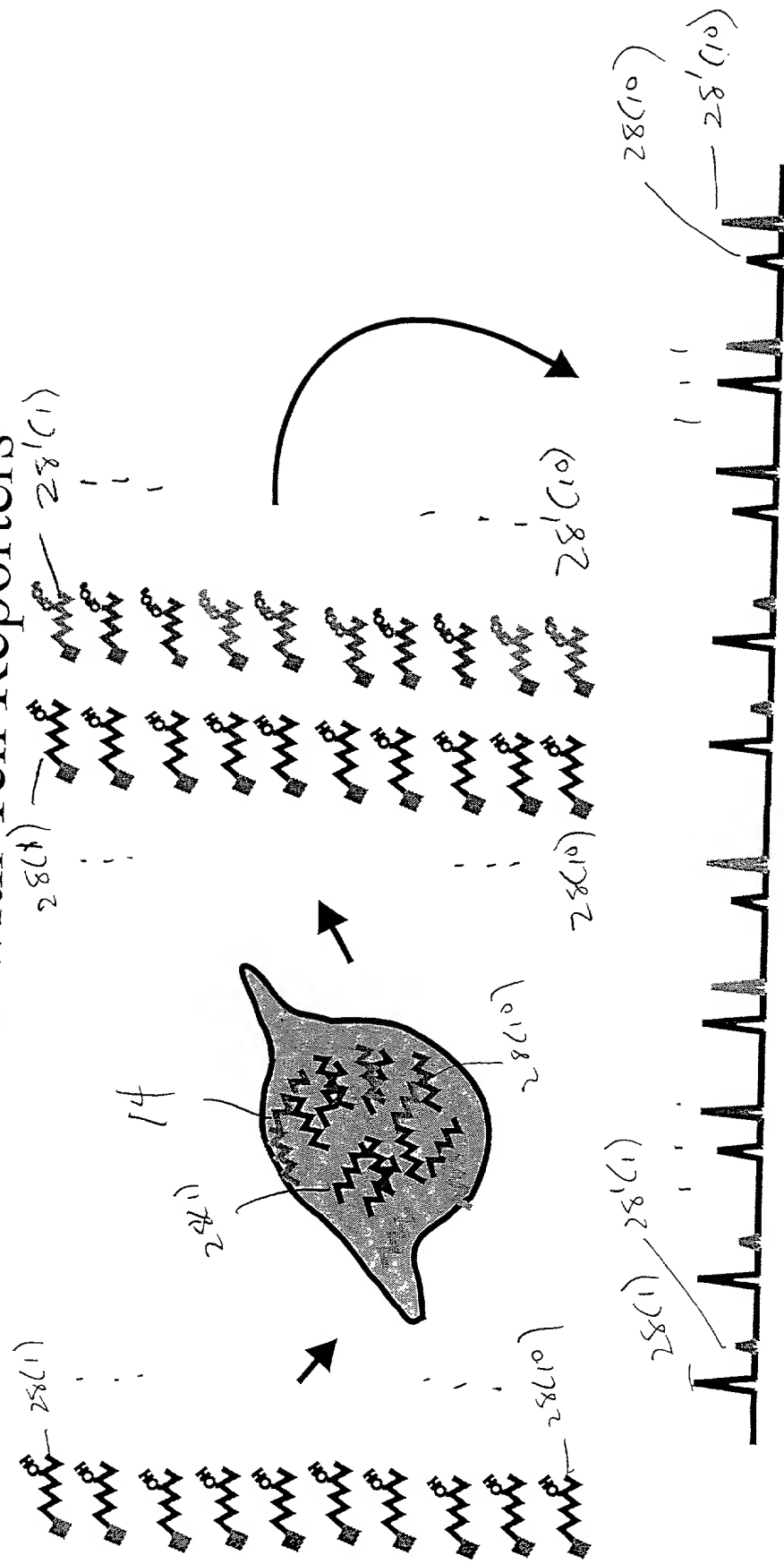


Fig. 18

Profiling Signal Transduction Pathways in Cells with Many Reporters

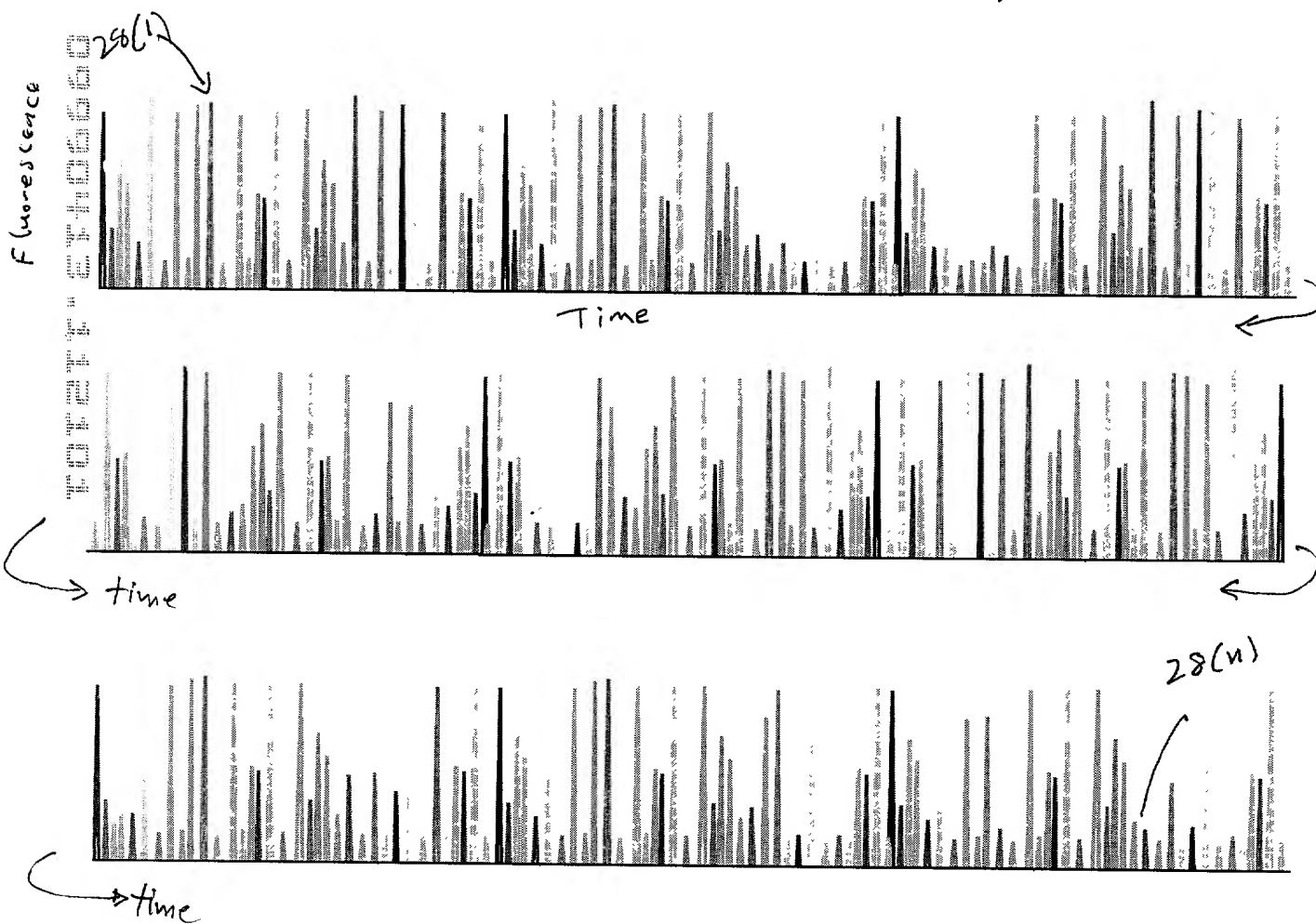
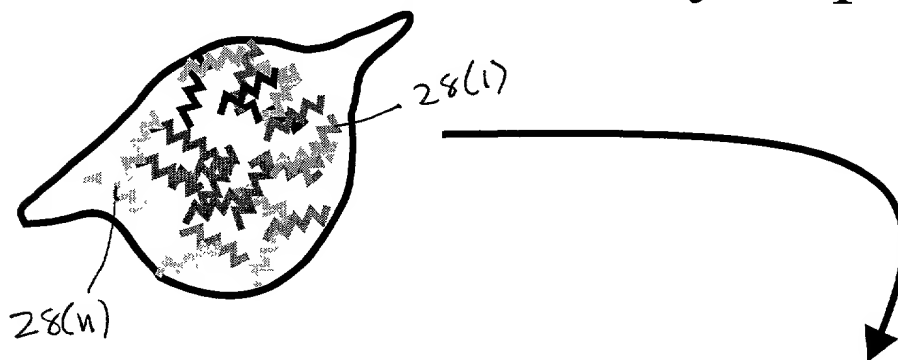


Fig. 19

FIG. 19 is a schematic diagram of a method for drug discovery and validation.

Applications

• Drug Discovery and Validation

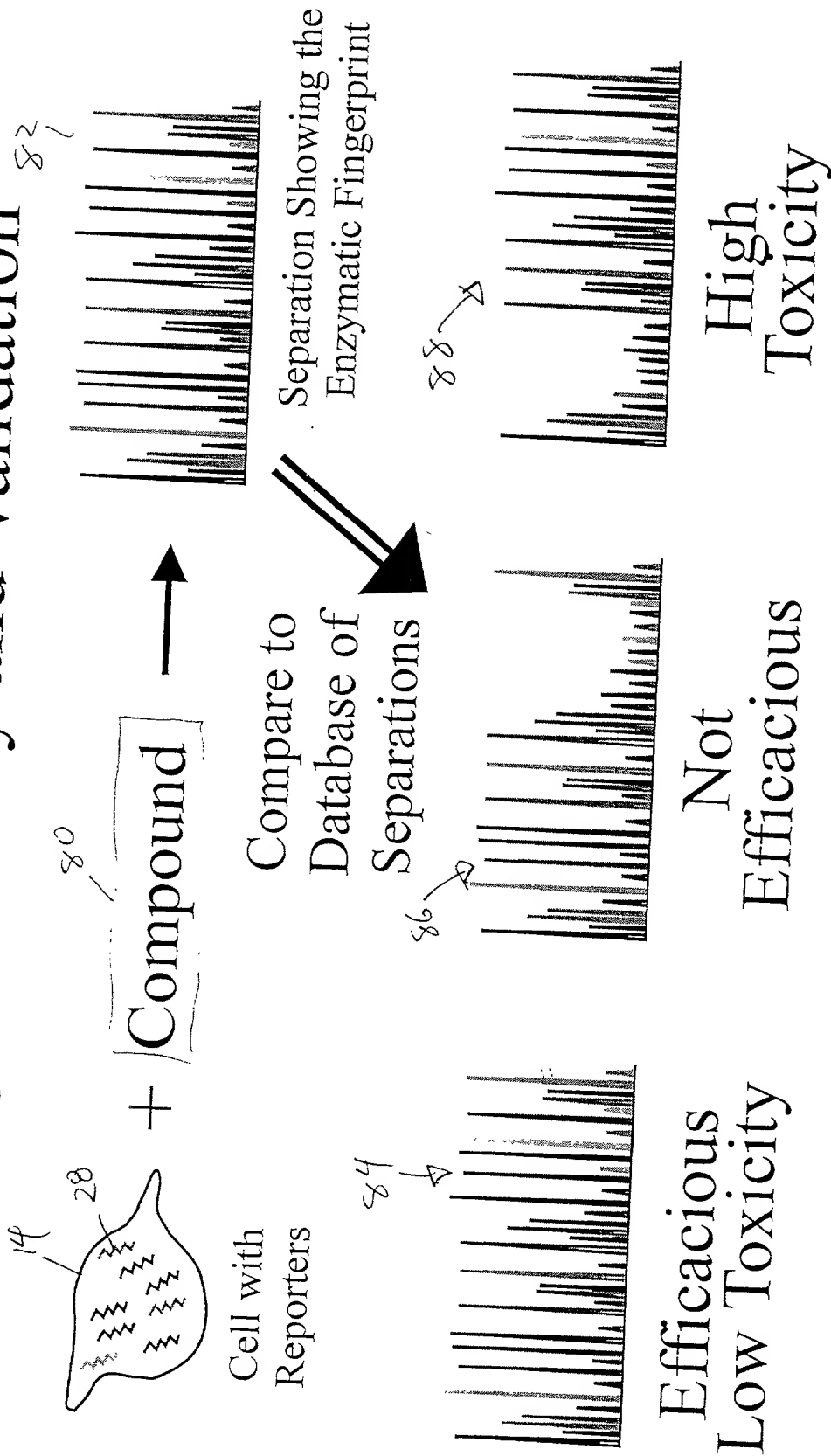


Fig. 20

Identifying the Cellular Targets of Compounds

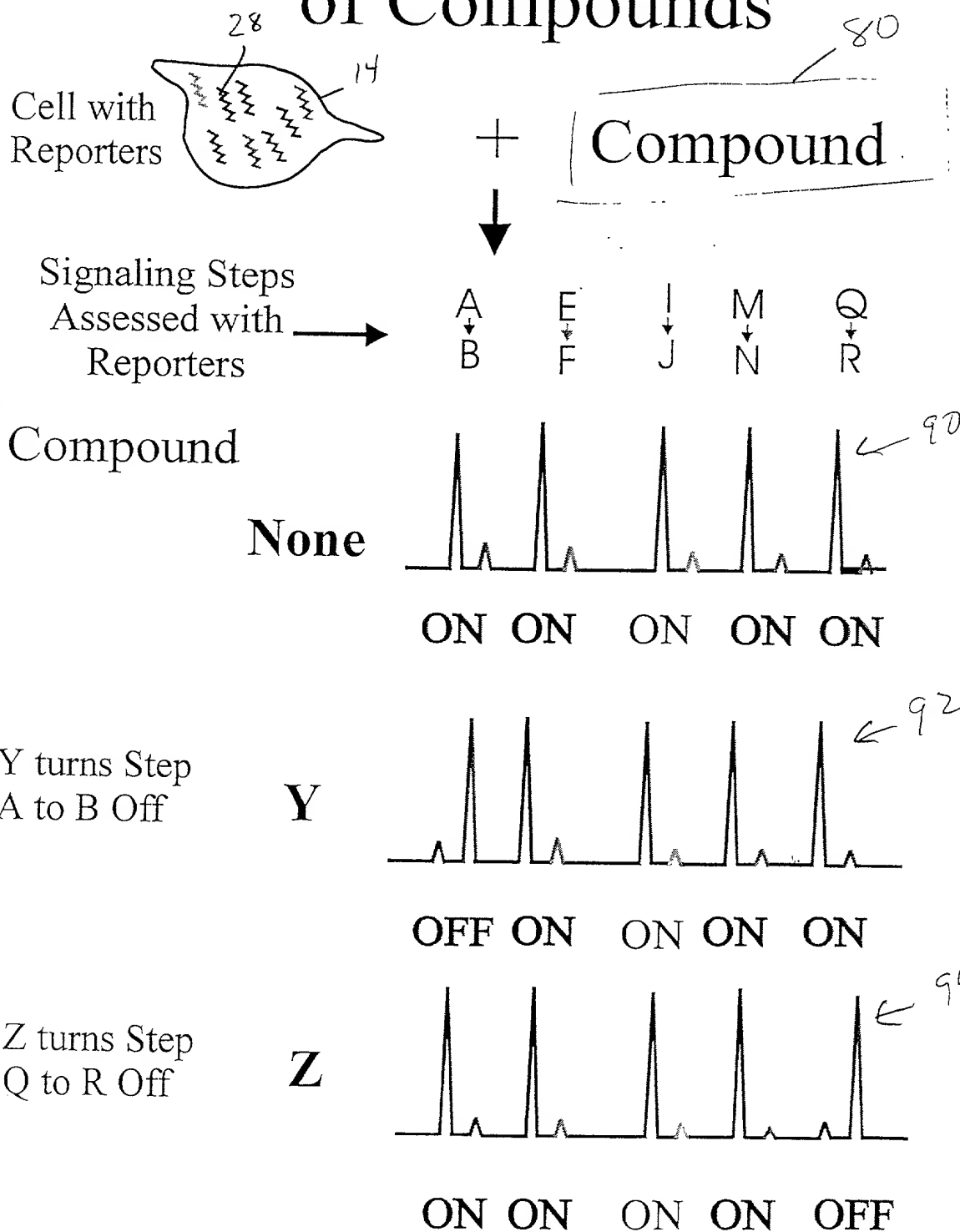


Fig. 21

Applications

•Diagnostics and Prognostics

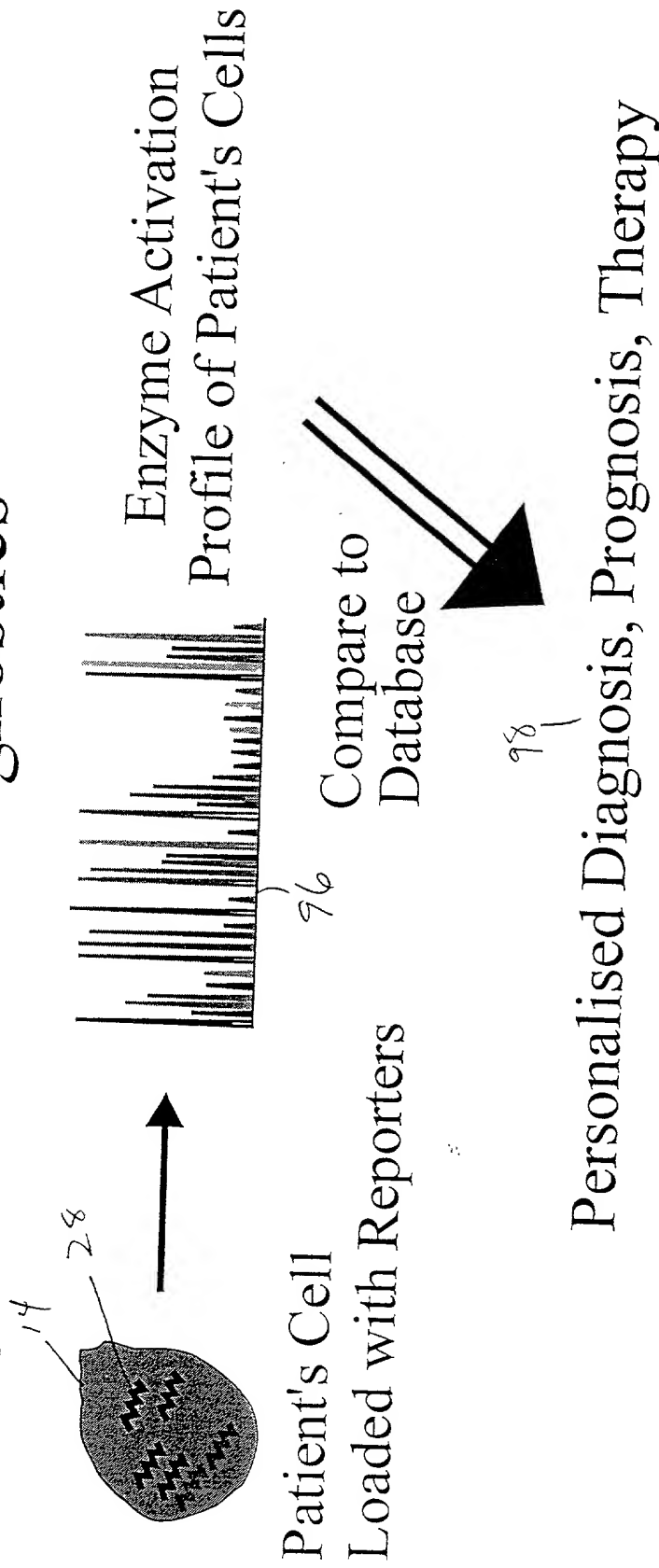
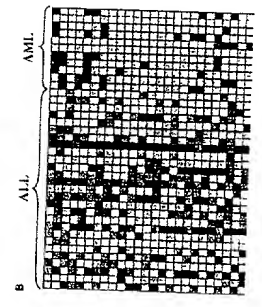


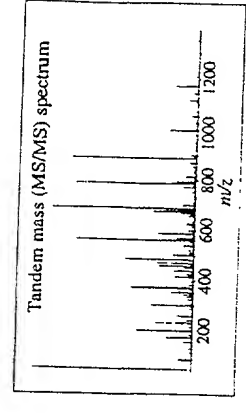
Fig. 23

Analysis of Biologic Systems



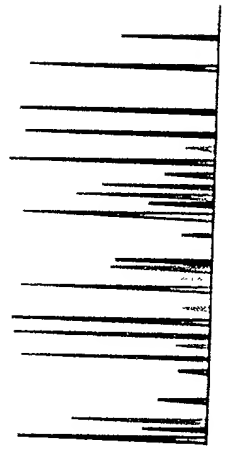
DNA Arrays

Genomics



Mass Spec.,
Protein Arrays

Proteomics



Protein Activity
Maps

Signaling

Fig. 24

Serial Analysis of Cells

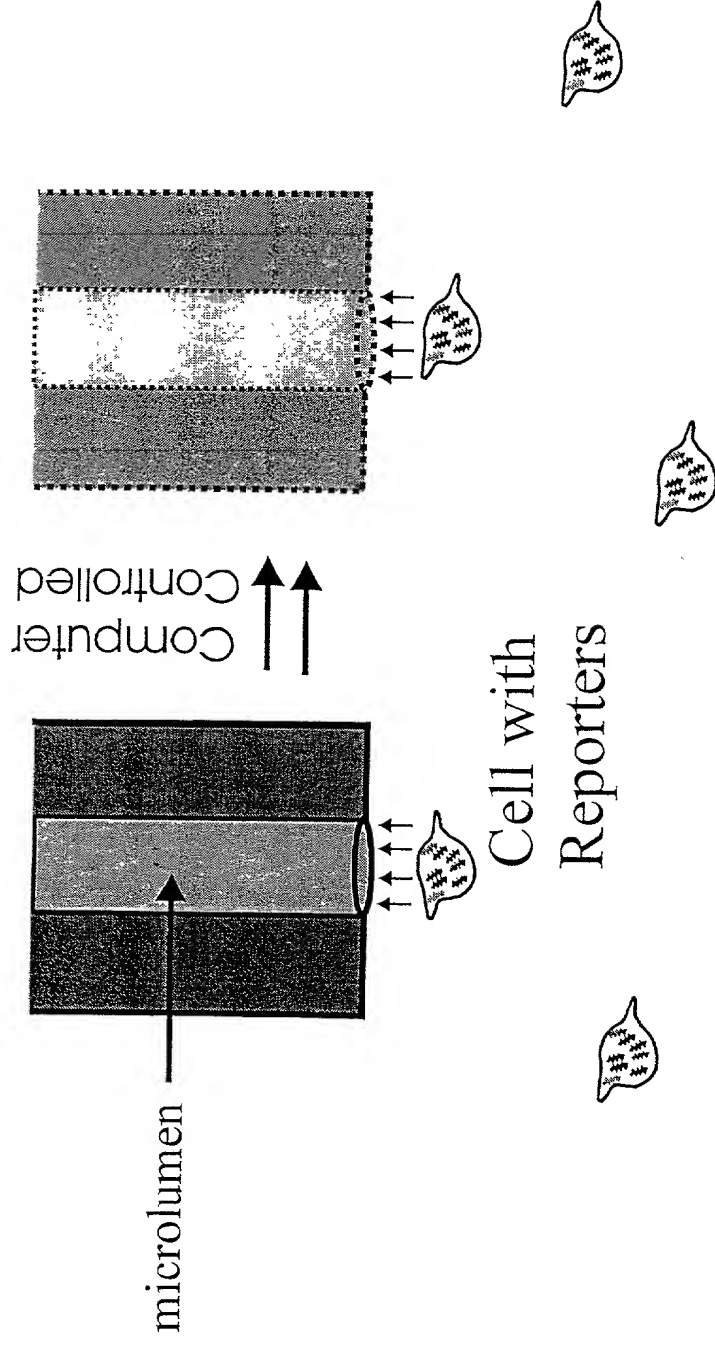
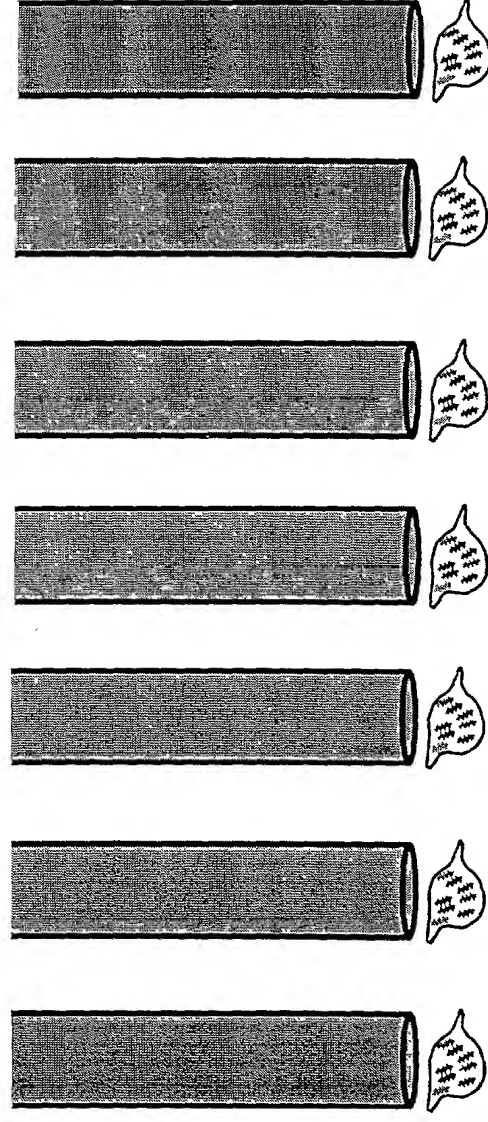


Fig. 25

Parallel Processing of Cells-

Arrays of Separation Channels



Computer-control of microlumen alignment
over cells, lysis, and/or other steps.